

REMARKS

Status of the Claims.

Claims 1-12, 20-29, and 31 are pending with entry of this amendment, claims 13-19, and 30 being cancelled and no claims being added herein. Claims _____ are amended herein. These amendments introduce no new matter. Support is replete throughout the specification (*e.g.*,).

Oath/Declaration:

The Examiner alleged that a new oath or declaration is required because of alterations to the addresses of inventors Joseph R. Pisegna and Stephan Wank. A new oath is presently being executed and will be forwarded when it becomes available.

Election/Restriction.

Pursuant to a restriction requirement made final, Applicants have canceled claims 13-19, and 30 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Information Disclosure Statement.

Applicants note with appreciation the Examiner's thorough consideration of the references cited in the Information Disclosure Statement (Form 1449) submitted on April 8, 2002.

Sequence Listing Rules.

Applicants note that the amendment filed May 14, 2002 regarding the sequence listing is acknowledged and that the CRF has been entered.

35 U.S.C. §112, Second Paragraph.

Claims 1-12, 21-29, and 31 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite as described below:

Re Office Action Paragraph 5:

Claims 1-12 were rejected as allegedly indefinite because claim 1 allegedly omitted an essential step because, according to the Examiner, the claim did not recite the end-point of the process. While Applicants respectfully disagree with the Examiner's assertion, to expedite prosecution, claim 1

is amended herein to recite". . . whereby the efficiency of said gastric proton pump inhibitor is increased" thereby obviating this rejection.

Re Office Action Paragraph 6:

Claim 2 was allegedly indefinite because the claim depends from itself. Claim 2 is amended herein to depend from claim 1 thereby obviating this rejection.

Re Office Action Paragraph 7:

Claims 2-10, 21,-29, and 31 were allegedly indefinite because of the use of the term " a pentagastrin, a gastrin, or analogue thereof". For the purpose of clarity, this phrase is rewritten as a Markush Group as follows:

" . . . administering to said mammal one or more agents selected from the group consisting of a pentagastrin, a gastrin, and a gastrin analogue . . . "

The dependent claims are amended to recite ". . . wherein said one or more agents is pentagastrin" in accordance with standard Markush practice thereby obviating this rejection.

Re Office Action Paragraph 8:

Claim 21 was rejected under 35 U.S.C. §112, first paragraph, as allegedly indefinite because the claims depends from a claim with a higher claim number. Claim 21 is amended herein to depend from claim 20 thereby obviating this rejection.

Re Office Action Paragraph 9:

Claim 22 was rejected under 35 U.S.C. §112, first paragraph, as allegedly indefinite because of the recitation of the word "or". The word "or" is deleted with entry of this amendment thereby obviating this rejection.

In view of the foregoing, amendment and comments, Applicants believe the rejections under 35 U.S.C. §112, second paragraph, are obviated and request withdrawal of these rejections. Applicants further note that the foregoing amendments do not alter the scope of the claimed invention..

35 U.S.C. §102.

Claims 1, 2, 5, 6, and 7 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Simon *et al.* (199) *Aliment Pharmacol Therap.*, 4: 239-245. Claims 1 and 12 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Murphy *et al.* (U.S. Patent 4,997,950). Applicants respectfully traverse.

A) Simon et al..

Simon *et al.* offers no teaching whatsoever indicating that pentagastrin, gastrin or a gastrin analogue increases the efficacy of a gastric H⁺/K⁺-ATPase pump inhibitor (PPI). Thus, the Examiner must be relying on inherency to support the stated rejection.

The Examiner is reminded that anticipation by inherency requires that:

- 1) the missing descriptive matter be "**necessarily present**" in the prior art reference and that
- 2) **it would be so recognized** by persons of ordinary skill in the art. [emphasis added] *Continental Can Co. v Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991)

In the instant case, claim 1, as amended recites:

1. A method of increasing the efficacy of a gastric H⁺/K⁺-ATPase pump inhibitor (PPI) in a mammal, said method comprising:
administering to said mammal one or more agents
selected from the group consisting of a pentagastrin, a gastrin, and a gastrin analogue, in conjunction with said gastric proton pump inhibitor **whereby the efficiency of said gastric proton pump inhibitor is increased.** [emphasis added]

There is nothing in Simon *et al.* that would lead one of ordinary skill to recognize that efficacy of a PPI could be increased by gastrin, pentagastrin, or a gastrin analogue. Siimon *et al.* simply investigate the efficacy of the PPI BY 1023/SF&F 96022. The PPI was administered to human volunteers that in whom acid secretion had been induced using pentagastrin. **Simon et al. does not show the effect of PPI BY 1023/SF&F 96022 in subjects that were not administered pentagastrin.** **Thus, Simon et al. cannot teach one of skill that the pentagastrin increased the efficacy of the PPI.**

Moreover, Simon *et al.* teaches the use of pentagastrin to stimulate gastric acid secretion, while PPIs are used to reduce/inhibit gastric acid secretion. Simon thus uses pentagastrin to induce the pathological state which is then mitigated by the administered PPI. In contrast, the presently claimed method contemplates the administration of gastrin, pentagastrin, or a gastrin analogue with the PPI to increase the efficacy of the PPI (*i.e.*, to reduce or inhibit the pathological condition).

In view of the foregoing, the use of pentagastrin, gastrin, or a gastrin analogue to increase the efficacy of a PPI would not be recognized by one of skill reading Simon *et al.* Accordingly the rejection of claims 1, 2, 5, 6, and 7 under 35 U.S.C. §102(b) in light of Simon *et al.* should be withdrawn.

B) Murphy *et al.*

Claims 1 and 12 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Murphy *et al.* (U.S. Patent 4,997,950). Applicants respectfully traverse.

The specification expressly states:

In particular, this invention pertains to the discovery that **administration of pentagastrin** (an agent that is typically used to increase acid secretion), in conjunction with a proton pump inhibitor (PPI) **will result in increased efficacy (e.g. prolonged effect and/or greater effect at reduced dosage) than use of the proton pump inhibitor alone.**

In addition, as indicated above, claim 1 recites

1. A method of **increasing the efficacy of a gastric H⁺/K⁺-ATPase pump inhibitor (PPI)** in a mammal, said method comprising:
administering to said mammal one or more agents selected from the group consisting of a pentagastrin, a gastrin, and a gastrin analogue, in conjunction with said gastric proton pump inhibitor **whereby the efficiency of said gastric proton pump inhibitor is increased.** [emphasis added]

In contrast, Murphy *et al.* simply states:

The conclusion is that these short peptides are potent and specific antagonists of gastrin, and they may be of use in the therapeutic control of acid secretion.

Such therapeutic control is achieved by the ability of the compounds of this invention to competitively inhibit the actions of endogenous gastrin. The following uses are illustrative:

Adjunctive therapy with drugs such as omeprazole which block the release of acid resulting in elevated levels of gastrin because of lack of suppression of gastrin release by acid;

Murphy *et al.* fails to teach that the disclosed peptides, when administered in conjunction with a PPI increase the efficacy of that PPI. One of skill in the art would appreciate that the PPI and the gastrin derivatives disclosed by Murphy *et al.* could function by different mechanisms and have no effect on each other. Thus, absent the teaching provided in the present application, one of skill in the art, reading Murphy *et al.* would not recognize the efficacy of the PPI is increased by the use of gastrin, pentagastrin, or a gastrin analogue.

The Examiner has failed to make a *prima facie* case of anticipation by inherency and, accordingly the rejection of claims 1 and 12 under 35 U.S.C. §102(b) in light of Murphy *et al.* should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,



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